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PCT/JP2003/007148

Translation

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference Y0321-PCT | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/JP2003/007148 | International filing date (*day/month/year*) 05 June 2003 (05.06.2003) | Priority date (*day/month/year*) 06 June 2002 (06.06.2002) |
| International Patent Classification (IPC) or national classification and IPC C12N 15/09, C12N 1/15, C12N 1/19, C12N 1/21, C12N 5/10, C12N 9/04, C12Q 1/68, G01N 33/50 | | |
| Applicant YAMANOUCHI PHARMACEUTICAL CO., LTD. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 09 October 2003 (09.10.2003) | 23 January 2004 (23.01.2004) |
| Name and mailing address of the IPEA/JP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/007148

## I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 6, 10

because:

☒ the said international application, or the said claim No. 6 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The invention of claim 6 concerns a method for treating or diagnosing the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☒ the description, claims or drawings *(indicate particular elements below)* or said claim No. 10 are so unclear that no meaningful opinion could be formed *(specify)*:

It is entirely unclear which specific compounds are included within the scope of the expression "substances obtained by the above screening method" used in claim 10 and which compounds are excluded. Therefore, the description of this claim is exceedingly vague. As a result, no opinion concerning this claim can be handed down.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 6, 10.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-5, 7-9 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 2, 7, 9 | YES |
| | Claims | 1, 3-5, 8 | NO |
| Industrial applicability (IA) | Claims | 1-5, 7-9 | YES |
| | Claims | | NO |

2. Citations and explanations

Document 1
WO 01/96390 A2 (CORIXA CORP) December 20, 2001, SEQ ID Nos. 1, 2, 21, 22, 41 and 42; Claims
Document 2
WO 00/28031 A2 (UNIV EMORY) May 18, 2000, SEQ ID Nos. 244 and 245; Claims
Document 3
WO 02/06515 A2 (DIADEXUS INC) January 24, 2002, SEQ ID Nos. 1, 2 and 84; Claims
Document 4
BABFI, B. et al., A mammalian $H^+$ channel generated through alternative splicing of the NADPH oxidase homolog NOH-1.
Science (2000) Vol. 287, No. 5450, p. 138-142
Document 5
SUHM YA. et al., Cell transformation by the superoxide-generating oxidase Mox1.
Nature (1999) Vol. 401, No. 6748, p. 79-82
Document 6
OSTRAKHOVITCH, EA. et al., Oxidative stress in rheumatoid arthritis leukocytes: suppression by rutin and other antioxidants and chelators.
Biochem Pharmacol. (2001) Vol. 62, No. 6, p. 743-746

Based on the description in document 4 cited in the international search report, the inventions of claims 1, 3-5, and 8 lack an inventive step.

Document 4 cited in the international search report describes a polypeptide, NOH-1 Lv, identified by Genbank Accession No. AF166328 that comprises an amino acid sequence that differs by only one amino acid from the amino acid sequence represented by SEQ ID NO: 2 of this application, and the gene for NOH-1Lv that differs by only one base from the base sequence represented by SEQ ID NO: 1 of this application. Furthermore, document 4 describes NOH-1Lv being a NADPH oxidase.

Generally speaking, on the priority date of this application, if a gene encoding a protein having a specific function was cloned, it was conventional technical practice to make additions, deletions and substitutions to that gene without losing the function and properties. In addition, expressing the gene that encodes the mutant polypeptide thus obtained in a suitable host, and screening for substances that inhibit the activity of that polypeptide by bringing the host cells into contact with test substances were widely practiced techniques before the priority date of this application.

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

As a result, based on the sequence of NOH-1Lv described in document 1, this examination finds that persons skilled in the art could easily conceive of obtaining a gene that encodes an amino acid sequence in which one or more amino acids are deleted, substituted, or added and a mutant polypeptide therefrom, expressing the gene that encodes the mutant polypeptide thus obtained in a suitable host, and screening for substances that inhibit the activity of that polypeptide by bringing the host cells into contact with test substances.

In addition, this examination finds that it is very likely that the mutant polypeptides thus obtained will include "polypeptides having an amino acid sequence in which one or more amino acids have been deleted from and/or inserted into the amino acid sequence represented by SEQ ID NO: 2" of the invention of claim 1 and will be specifically expressed in patients with rheumatoid arthritis. Therefore, the above invention does not provide any unforeseeable outstanding effect.

None of the documents describes or suggests the inventions of claims 2, 7, and 9, and therefore these inventions are novel and involve an inventive step.

None of the documents describes the polypeptide comprising the amino acid sequence identified as SEQ ID NO: 2 or the fact that this polypeptide is specifically expressed in rheumatoid arthritis. Moreover, none of the documents describes or suggests the use of the polypeptide comprising the amino acid sequence identified as SEQ ID NO: 2 of this application or the use of a gene containing a base sequence of polynucleotides that encode a polypeptide specifically expressed in RA patients, including amino acid sequences that are 95% or more homologous with the amino acid sequence represented by SEQ ID NO: 2.